A STUDY ON INCIDENCE, RISK FACTORS AND TREATMENT STRATERGIES IN CASES OF PROSTHETIC VALVE THROMBOSIS

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CERTIFICATE

This is to certify that the dissertation titled **"A STUDY ON INCIDENCE, RISK FACTORS AND TREATMENT STRATERGIES IN CASES OF PROSTHETIC VALVE THROMBOSIS"** is the bonafide original work of **Dr. SUNDAR. C,** in partial fulfillment of the requirements for D.M; Branch– II (Cardiology) Examination of the Tamilnadu Dr. M.G.R Medical University to be held in AUGUST 2013. The Period of study was from April 2012 to March 2013.

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DECLARATION

I hereby solemnly declare that the dissertation titled "**A STUDY ON INCIDENCE, RISK FACTORS AND TREATMENT STRATERGIES IN CASES OF PROSTHETIC VALVE THROMBOSIS"** was done by me at Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai-3 during April 2012 to March 2013 under the guidance and supervision of my Prof & HOD Prof. Dr. V.E. Dhandapani D.M; The dissertation is submitted to the Tamilnadu Dr. M.G.R. Medical University towards the partial fulfillment of requirement for the award of D.M; degree (Branch-II) in Cardiology.

Place: **Dr. Sundar. C**

Date: **SIGNATURE OF THE CANDIDATE**

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CONTENTS

INTRODUCTION

Prosthetic valve thrombosis (PVT) is a serious and the most dangerous complication, the incidence varies in various parts of the world. The risk factors are multifactorial. The technique of surgical valve replacement introduced in earlier 1960s markedly changed the prognosis of patients having valvular heart disease. Around 300 000 valve replacements are done all over the world each year with both mechanical as well as bio prosthetic valves. In spite of substantial developments in surgical techniques and the design of prosthetic valve over the past decades, replacements of valves have not provided a cure. The durability, hemodynamics and thrombogenicity of the prosthetic valves affect the prognostic outcome of valvular heart disease patients who undergo replacement of valve. Most of the complications related to prosthetic valves can be prevented by optimal selection of prosthesis and its follow up management. The ideal prosthetic valve should be having the same characteristics of the native valve with good hemodynamics, extensive durability, resistance to thrombosis, and suitable implantability. But, such ideal prosthesis has not been so far found, and the presently available prosthetic valves have many limitations. The treatment strategies such as surgery and fibrinolysis remain the main stay. Trans thoracic echocardiography (TTE), Transesophageal

echocardiography (TEE) and sometimes fluoroscopy aids in diagnosis. Prosthetic valve thrombosis is diagnosed when any thrombus, in the absence of infection, adherent over the operated valve or near it, obstructing part of the blood flow or interfering function of the valve.. TEE has limitation to distinguish between pannus and infected vegetations from thrombi. In such instances, clinical aspects are helpful. The incidence of PVT is estimated to be 0·1 to 6% per patient-year, of which aortic PVT -0·2% per patient-year, mitral PVT – 1.8% per patient-year. But the incidence should be higher, as TTE and TEE reveals almost all cases and of which half are asymptomatic. Various therapeutic modalities are recommended for PVT. Surgical treatment is indicated for 69%, according to their NYHA class and emergency situation. Thrombolysis is also recommended as a treatment option, showing more than 80% success and fewer complications. There are no absolute contraindications besides classical contraindications such as early postoperative period large thrombi, pregnancy for thrombolysis. Streptokinase protocols have been used. Heparin can also be a primary treatment option for nonobstructive PVT, but fibrinolysis is more superior. If the size of the thrombi attached to the leaflets is larger, heparin is not helpful. During heparin therapy TEE should be done, as there may be increase in the size of thrombi and can cause obstruction.

Thrombolysis, if there are no contraindications can be recommended as first-line of treatment. Surgery is recommended for patients for whom there is contraindication for thrombolysis or where it's deemed to be ineffective. Prosthetic valve thrombosis (PVT) can endanger the life for which therapeutic options remain controversial. It may be salient to review the definitions, tools for diagnosis and their limitations, the epidemiology of PVT before comparing, discussing the different therapeutic modalities that are available for treatment of this condition.

AIMS AND OBJECTIVES

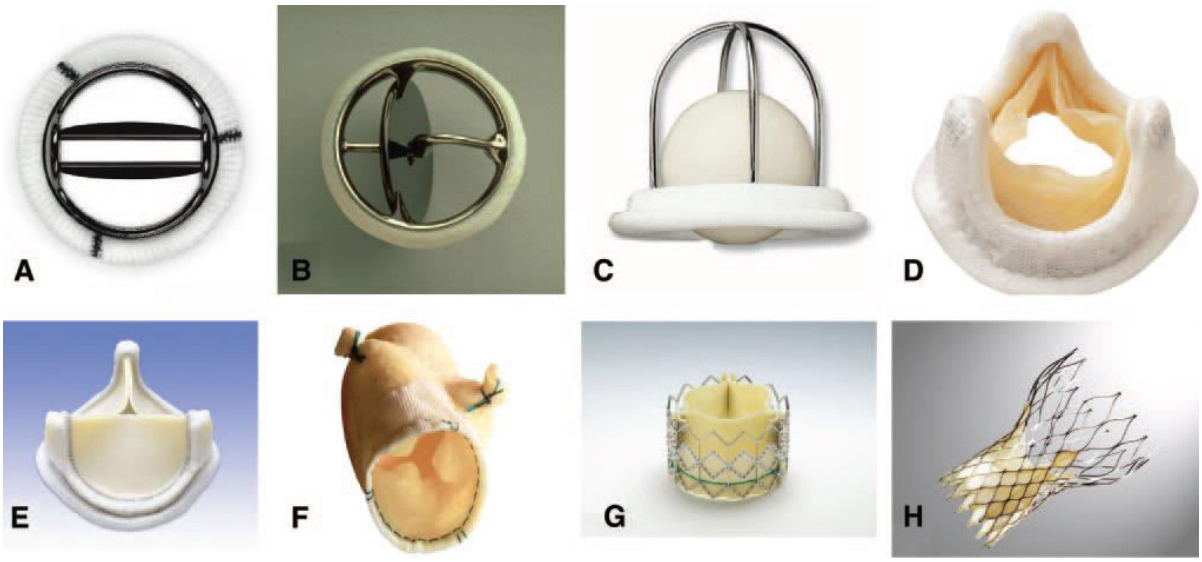
To study the incidence, risk factors of patients presenting with prosthetic valve thrombosis.

To study the treatment strategies of patients presenting with prosthetic valve thrombosis**.**

REVIEW OF LITERATURE

Prosthetic valve thrombosis (PVT) could be a rare however a dangerous complication of prosthetic valve implantation. The morbidity and mortality of this disease is high and needs speedy diagnostic analysis. However, diagnosis is often difficult, primarily as a result of varied presentations and therefore the amount of valvular obstruction. Transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE) and cinefluroscopy for mechanical valves are the common diagnostic tools. Though surgery is the preferred treatment in obstructive PVT still other options are available. The various treatment options offered for PVT are primarily based on the presence of obstruction of the valve orifice, by location of the valve (right or left sided), and clinical mode of presentation. Therefore, treatment of left-sided PVT can be different from right-sided PVT or non obstructive PVT.

Figure showing various types of prosthetic valves



EPIDEMIOLOGY:

Thromboembolism, are frequent which occur at an incidence of 0.8–6.1% patient years [1]. PVT which are non obstructive could be a comparatively frequent finding in the post operative periods [2]. Though these are non-obstructive small thrombi, they emphasize the treatment with anticoagulants in the post operative periods [3]. Bioprosthetic valve thrombosis could be a rare phenomenon compared to mechanical valves [4]. PVT of bioprosthesis is sometimes diagnosed within the early post operative period, as suture zone endothelialisation isn't nonetheless complete. Hence, anticoagulants are advised for the first three months after bioprosthetic valve implantation, especially for prostheses at mitral position.

PHYSIOPATHOLOGY:

Based on Virchow's triad, the factors which predisposes to thrombosis are classed into hemodynamic, endothelial and haemostatic elements [5]. Biocompatibility of the prosthetic device is represented by endothelial factors and interaction between the prosthetic device and the suture zone. Endothelialisation and tissue cicatrisation characteristically need a couple of weeks to be completed. Haemodynamic factors represents haemodynamic characteristics of the prosthetic device, and cardiac hemodynamics overall. Though the profile of recent generation bileaflet mechanical valves is basically superior thereto of previous generation prosthetic valves (and so related to a lower incidence of thromboembolism), flow turbulence at localised regions will still develop and result in stasis and formation of thrombus. Additionally, the prosthetic device location is a crucial factor in thrombogenicity. Tricuspid mechanical valve obstruction is twenty times frequent than PVT of left side.

Also PVT in mitral location is more frequent than occlusion of prosthetic device in aortic position for haemodynamic reasons. Thrombosis, significantly in low flow states or decreased cardiac output situations is also due to hemodynamic reasons. The adequacy of

anticoagulant treatment involves haemostatic factors. Hence, the immediate post operative period represents a specific challenge with the necessity to balance the danger of over anticoagulation and associated bleeding complications with under-anticoagulation and thromboembolic complication.[6] Equally, stopping of anticoagulants for non-cardiac surgery and pregnancy are significant risky situations [7,8]. Pathology Although PVT presents as acute thrombosis, its mostly subacute or chronic development. Apparently, recent literature have shown the higher reports of pannus formation (46–76% of cases), that is additionally related to the risk of thrombus formation. Pannus formation is sometimes discovered near suture and may be situated on either side of the prosthetic device, degrees of evidence of obstruction [9]. Lastly, obstruction may result from vegetation during endocarditis of prosthetic valve.

How to diagnose:

Clinical scenario:

The clinical presentation is extremely variable, based upon if the obstruction is present or not. PVT with severe obstruction is usually presents as heart failure, whereas PVT which is non obstructive is commonly present incidentally or embolism. Obstruction which is partial will present as breathlessness or embolic phenomenon and infrequently

fever. Diagnostic blood cultures ought to be performed in the presence of fever to diagnose infectious carditis.

Biochemical tests:

Traditional markers of inflammation and levels of anticoagulation are done through biochemical analysis. D-dimer levels could also be elevated. Meticulous clinical examination ought to be performed, to look for muffling of valvular sounds, appearance of new murmur which can be stenotic or regurgitant.

Fluoroscopy:

All mechanical prosthetic valves offered are radiopaque, cinefluoroscopy is an important diagnostic tool for analysis of PVT. However, this method is not useful in differentiating pannus from thrombus. Hence, further diagnostic work up should be done [10].

Trans thoracic echocardiography:

By TTE, prosthetic device can be directly visualised and measure transvalvular gradients. It is a vital part in diagnosis. A customary complete examination ought to be performed, with important attention given to measuring transvalvular flow, gradient, and visualization of prosthetic device [11]. Using colour Doppler, abnormalities in the flow

across prosthesis or central regurgitation, which indicates valve closure of the valve, are often discovered. Transprosthetic gradients and effective orifice area (EOA) are measured using continuous wave Doppler. Measurement of cardiac output and pulmonary artery pressure should be done. Direct signs of PVT are abnormal mobile prosthetic device or thrombus at or near the valve apparatus visualisation. For mitral prostheses, A mean gradient >8 millimetre of mercury and an EOA of <1.3 cm^2 suggests PVT. For prostheses in aortic position, PVT criteria are a mean gradient >45 millimetre of mercury and an obstruction index <0.25. In the event of prosthetic aortic valve which are smaller in size, identification is tough taking in to the fact that they normally have elevated gradients, owing to turbulent flow across the orifice which is small and causing patient–prosthesis match (PPM) [12,13].

"Silent Doppler PVT" is the term used to specify during low cardiac output situation where transvalvular gradients can be normal and still there may be obstruction of prosthesis [14].

Trans esophageal echocardiography:

In cases of large PVT, TEE may not be required. In most of the cases, TEE can offer vital further diagnostic info, which can additionally guide treatment [15, 16]. Direct signs of PVT are immobility or reduced

leaflet quality, and therefore the thrombus on either facet of the prosthetic device, with or while not obstruction.

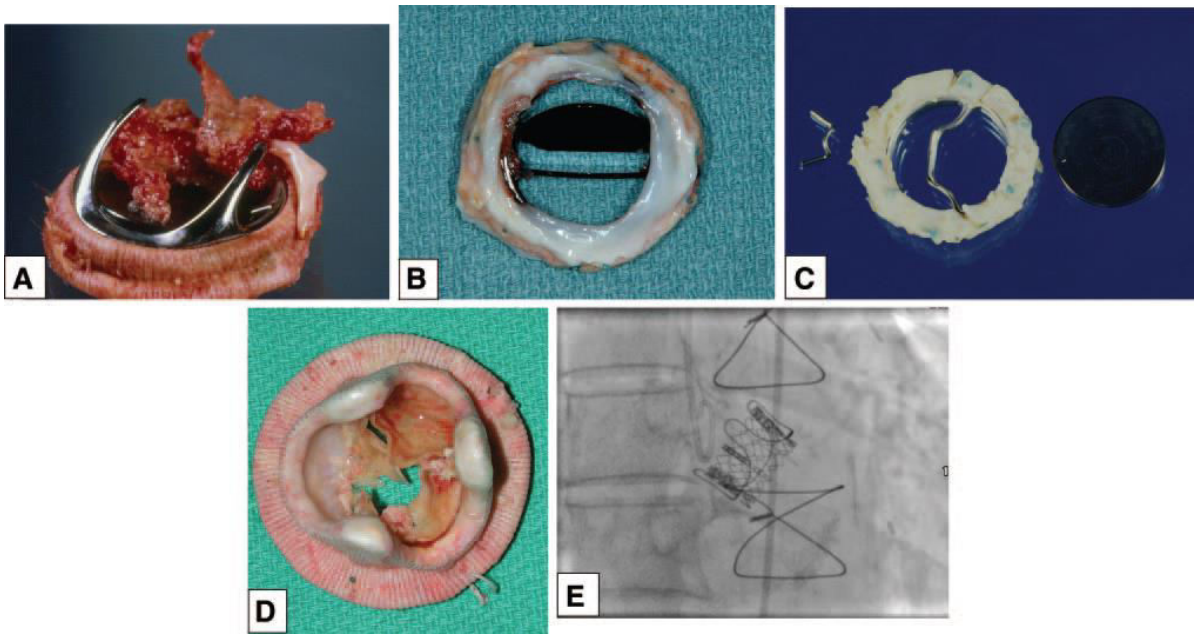
A fibrous pannus which is usually in annular location needs to be differentiated from thrombi. Formation of pannus is more on aortic rather than prostheses on mitral position. Indirect signs of PVT by TEE are usually the non visualisation of the physiological prosthetic device regurgitation, the visualization of central regurgitation, and left atrial spontaneous contrasts in echocardiography.

TEE also has some major limitations: prostheses at aortic location are difficult to be evaluated than prostheses at mitral location, and as also the ventricular side of the prosthesis at mitral location. It is additionally vital to differentiate smaller thrombus from strands or sutures. Strands are the protein structures, showing as fine usually <1 mm, filiform, mobile echos of differential length (approximately ten millimetre), and frequently discovered on the atrial part of mitral prostheses. Though the ideal nature of those strands still unknown, literature states that there is no significant risk of embolism.

Finally, it is to be emphasized the vital role of TEE in deciding treatment methods. For PVT in the left sided valves, surgery is preferred for larger thrombus, as thrombolysis increases the risk of embolism. The

PRO-TEE register suggest that a thrombus with a size of >.0.8 cm2 and a previous history of cerebrovascular event as the significant factors for the anticipation of complications of fibrinolysis [17]. In non-obstructive PVT, the main stay of therapy is optimal medical treatment, unless there is a very larger or freely mobile thrombus. TEE is additionally useful in differentiating a pannus from thrombus, and in deciding size of the thrombus accurately. Thrombosis of a bioprosthetic valves encompasses a similar clinical presentation thereto of mechanical PVT. In cases of PVT, TTE can demonstrate abnormal transvalvular gradients. TEE is more sensitive than TTE for the identification of thrombosis of bioprosthesis.

Figure showing various disease process affecting prosthetic valves



TREATMENT:

Once PVT is diagnosed, treatment modalities must be decided such as surgery in the form of thrombectomy or valve replacement, thrombolysis, heparin, or anticoagulation dose adjustments or antiplatelets. Treatments are often optimized based on the presence of obstruction and prosthetic device location. The prosthetic device type doesn't impact treatment options, because the selection between surgical and medical treatment depends on location of the prosthesis, size of the thrombus and clinical situation. The introduction of TEE has paved the way for the best treatment modality for non-obstructive PVT.

Treatment is often done as per the size of the thrombus:

1. For non-obstructive thrombi of size >5mm, surgery is indicated in cases of medical management failure (heparin), especially when the thrombus is large, pedunculated and mobile [2, 6, 18].

2. For smaller non-obstructive thrombi of <5mmi, preferred strategy is medical treatment. Treatment with heparin is continued for seven days with repeat TEE to gauge therapeutic effectiveness, or adjustment of anticoagulant medication and introduction of aspirin at a lower dose (100 mg). thrombolysis can be given successfully for smaller nonobstructive thrombi, however with a risk of embolism.

Obstruction of a mechanical prosthetic device needs treatment aggressively (surgery or thrombolysis), as there is always sub therapeutic anticoagulation levels in these patients.

There are only few guidelines in the literature regarding PVT management (level two recommendations). American of Cardiology/ American Heart Association recommend surgery as the treatment of choice for left-sided PVT [19]. Thrombolysis is recommended for clinically and hemodynamically unstable patients (NYHA III or IV), with high surgical risk or contraindications to surgery. It can also be recommended for hemodynamically stable patients with functional class of I, II and a smaller thrombus following heparin treatment failure.

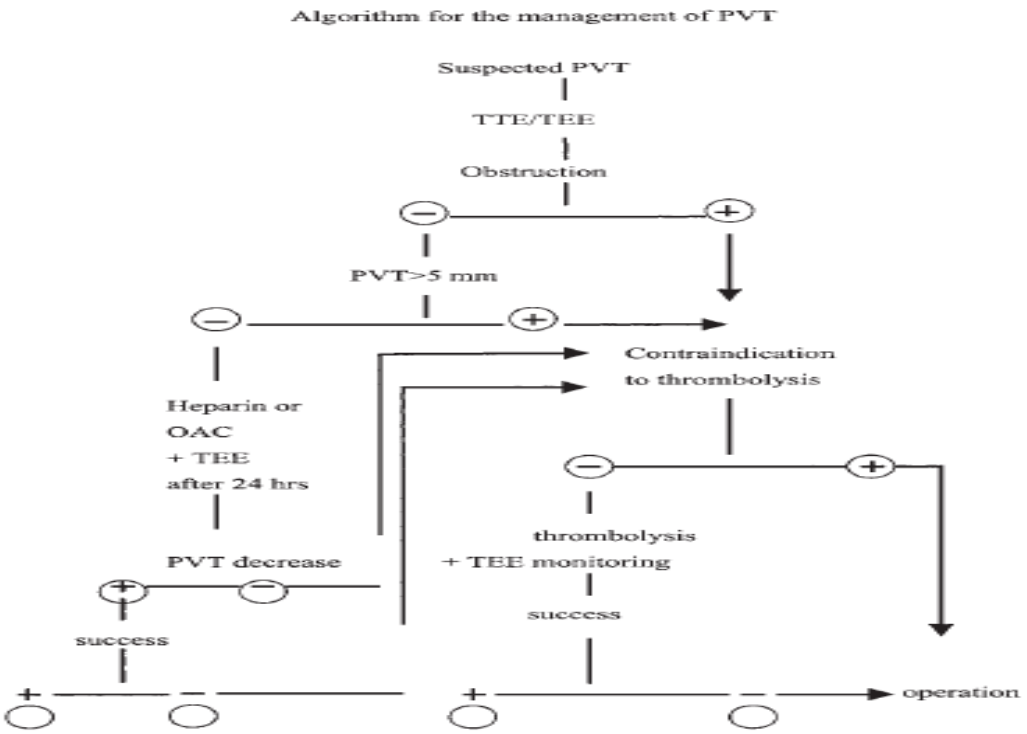
Right-sided PVT:

Mechanical prosthetic valves are seldom implanted in the right side of heart, primarily as a result of their increased thrombogenicity. Obstruction of pulmonic or tricuspid prosthetic device is a situation for thrombolysis [20]. Surgery is indicated for right sided PVT in cases of failure of thrombolysis.

Left-sided PVT:

Surgery is the treatment of choice for left sided PVT, with thrombolysis reserved for exceptional situation [21, 22, 23]. Traditionally, surgery was considered as a high risk, but with the recent advancement in the operative procedure and anaesthesia, prognosis has been considerably improved. . Surgery can be replacement of the valve or thrombectomy. Thrombolysis was introduced as a reasonable alternative in the early 1970s. A recent review by Lengyel et al found thrombolysis to be efficacious in 82% cases, however with an associated 10% morbidity and a 12.5% risk of emboli [24]. Thus because of this high complication rate thrombolysis is recommended as a second line therapy. A simple algorithmic program for the management of PVT is as follows

Figure shows algorithm for treatment of PVT



Fibrinolytic treatment protocols:

There are no accepted guidelines regarding the most effective thrombolytic programme. Two different strategies are suggested. In patients with unstable hemodynamics, ‘‘rescue’’ thrombolysis is preferred employing a ‘‘short protocol’’ with either: 1. Streptokinase 1500 000 U in sixty minutes while not heparin. 2. Recombinant tissue plasminogen activator (rtPA) ten mg bolus + ninety mg in ninety minutes. In patients with stable hemodynamics, another longer term strategy is commonly preferred: Streptokinase 500000 IU in 20 minutes followed by

150000 IU over 48 hours without heparin or Urokinase 4500 U/kg/h over twelve hours, or 2000 U/kg/h + heparin over twenty four hours. rtPA ten mg bolus, followed by 50mg throughout the first one hour, twenty mg in the second hour and twenty mg in the third hour. Another thrombolytic agent can be used in case of failure of primary agent. Embolic complication is the dreaded risk of thrombolytic agents. TTE has a vital role in selection of patient for ultimate thrombolytic treatment. Thrombolysis has greater effectiveness for recent smaller thrombi

SUBJECTS AND METHODOLOGY

48 patients who were admitted in the department of cardiology, Rajiv Gandhi government general hospital, Chennai, with signs and symptoms of prosthetic valve thrombosis were included in the study. These patients had prosthetic valve implanted for severe rheumatic heart disease.

Inclusion criteria	Patients who are diagnosed to have prosthetic valve thrombosis.
Exclusion criteria	Patients with prosthetic valves but not fulfilling the criteria for prosthetic valve thrombosis. Not willing to sign consent form
Investigation details	1) Mode of clinical presentation. 2) ECG, Echocardiography(Trans thoracic and Trans esophageal) 3) Fluoroscopy

The incidence and risk factor, clinical profile of patients who are presenting with prosthetic valve thrombosis and their treatment strategies were analysed. They were on anticoagulants and were in follow up.

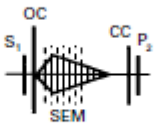
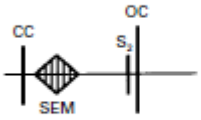
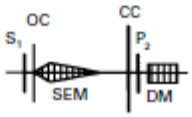
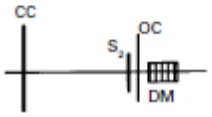
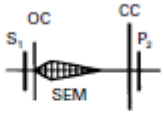
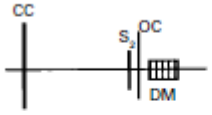
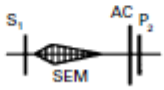
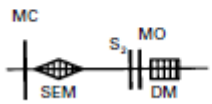
Patients with prosthetic valves and not fulfilling the criteria for PVT and those not willing to sign the consent form were excluded from the study.

Meticulous history was taken and risk factors predisposing to the PVT were recorded. Clinical examination was done and various presentation pattern of PVT were analysed. Investigational workup with electrocardiogram, echocardiography with both Trans Thoracic and Trans Esophageal mode were done in all patients to diagnose PVT. In all cases fluoroscopy was also done to both diagnose and to assess the treatment success. Preoperative clinical data, initial valve procedure and complications if any were recorded. Several factors such as the risk factors for PVT development, including sex, aortic versus mitral position, and single versus double-valve replacement, time duration since the valve replacement will be analyzed.

Clinical criteria used to suspect PVT:

Muffling or absence of prosthetic valve sounds was taken as an indirect sign of PVT.

Figure showing the normal and abnormal auscultatory findings in patients with prosthetic valves

Type of Valve	Aortic Prosthesis		Mitral Prosthesis	
	Normal Findings	Abnormal Findings	Normal Findings	Abnormal Findings
Caged-Ball (Starr–Edwards)		Aortic diastolic murmur Decreased intensity of opening or closing click		Low-frequency apical diastolic murmur High-frequency holosystolic murmur
Single-Tilting-Disk (Bjork–Shiley or Medtronic–Hall)		Decreased intensity of closing click		High-frequency holosystolic murmur Decreased intensity of closing click
Bileaflet-Tilting-Disk (St. Jude Medical)		Aortic diastolic murmur Decreased intensity of closing click		High-frequency holosystolic murmur Decreased intensity of closing click
Heterograft Bioprosthesis (Hancock or Carpentier–Edwards)		Aortic diastolic murmur		High-frequency holosystolic murmur

Echo criteria for diagnosing PVT:

By Philips HD 7 echo machine two-dimensional and Doppler echocardiographic studies were done; the system has 3.5 and 2.5 transducers (2- dimensional echocardiography), and 2.5 MHz transducers

for pulsed and continuous wave Doppler. A thorough 2-D echocardiographic examination was performed to view the prosthesis in many cross-sectional views. Continuous wave Doppler mode was used to measure the flow across the prosthetic valves. Peak pressure gradients were obtained from peak velocities by modified Bernoulli equation: P=4 xV2; mean pressure gradients were obtained with the software in the echo machine. Pressure half-time method was used to calculate the effective mitral orifice area.

TEE was done with 5 MHz multiplane probes. Criteria for mitral PVT were: evidence of thrombus with or without altered mobility of the disk(s) and pathological regurgitation through the prosthesis. Thrombus was defined as a “distinct mass of abnormal echoes attached to the prosthesis and clearly seen throughout the cardiac cycle”.

Echocardiographic criteria to diagnose mitral prosthetic valve obstruction:

	Normal	**Possible**	**Significant**
Peak velocity	<1.9	1.9-2.5	≥ 2.5
Mean gradient (mm Hg)	≤ 5	6-10	>10
VTI prmv/VTI LVO	<2.2	2.2-2.5	>2,5
EOA (cm2)	≥ 2	1-2	<1
PHT (ms)	<130	130-200	>200

Echocardiographic criteria to diagnose aortic valve PVT:

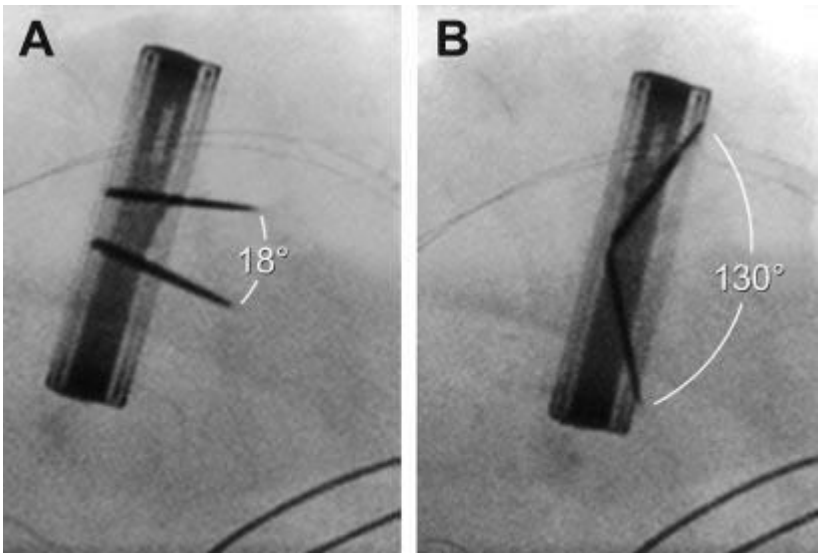
Peak velocity	**Normal**	**Possible**	**significant**
Peak velocity	<3	3-4	>4
Mean gradient	<20	20-35	>35
DVI	≥ 0.30	0.29-0.25	<0.25
EOA (cm2)	>1.2	1.2-0.8	<0.8
Contour of jet	Triangular early peaking	Triangular to intermediate	Rounded symmetrical
AT (ms)	<80	80-100	>100

A diagnosis of pannus formation was made when fixed, bright echodense structures, sometimes containing focal calcific deposits, were present primarily along the valve ring with extension into the valve orifice.

Fluoroscopic criteria for diagnosing PVT:

Fluoroscopic criteria for prosthetic valve obstruction were: persistent restriction of leaflet(s) motion with calculated opening angle greater than the mean value (_2SD) obtained in a reference group of patients with normally functioning valve of the same type. Opening and closing angles were defined as the distance between the 2 leaflets in the fully open and closed position.

Figure showing opening and closing angle measurement by fluoroscopy



Echo criteria for successful thrombolysis:

Patients with obstructive thrombus, and those with nonobstructive thrombus, who either had a history of embolization or had a large thrombus mass (>10 mm base diameter and/or >5 mm mobile segment length) were accepted as candidates for thrombolysis. Patients with large thrombus were not excluded. Thrombolytic treatment was contraindicated in patients with bleeding tendency and in those with expanding or hemorrhagic cerebral infarcts. Streptokinase (SK) was the agent used in all patients who were eligible for thrombolysis. Loading dose of SK was used. 2, 50,000 units was used as a loading dose followed by 1, 00,000 units per hour for 24-48 hours. Heparin as an infusion given after thrombolysis and overlapped with Acenocoumarol till the target INR reached >2.5.The response to thrombolytic treatment was defined as a complete success "when significant narrowing of the valve (based on hemodynamic measurements) was no longer present and a >75% reduction in largest diameter of the thrombus mass was achieved. For nonobstructive thrombi, a reduction by>75% in thrombus diameter or complete lysis of the mobile portion of the thrombus" was required as criteria for complete success. Clinically reduction in the severity of functional class, return of valve click sounds, echocardiographically by reduction of gradient and by fluoroscopy return of normal disc motion

.The positive responses that were less than “completely successful” were accepted as partial success. Treatment response was graded incomplete if there is a significant clinical improvement without complete recovery of disc or leaflet motion on fluoroscopy and/or TTE and graded as failure if there is no clinical improvement, in many cases associated with death or complications.

Surgery was done for the patients with large thrombi, mobile thrombi, shock, high risk for thrombolysis such as history of hemorrhagic stroke, active internal bleeding and severe hypertension at presentation (>200/120mmHg).

OBSERVATIONS AND RESULTS

48 patients were admitted with signs and symptoms of prosthetic valve thrombosis. Out of which 35 patients were males and 13 were females with the age ranging from 25-48 years. Overall 38 patients (males: 30, females: 8) were from rural areas and the remaining (males:5, females:5) were from semi urban areas. 30 patients (males: 20, females: 10) had prosthetic valve implanted in mitral position, 17 patients (males: 14, females: 3) had aortic valve prosthesis and one male patient had double value (both mitral and aortic) replacement. 35 patients (males: 26, females: 9) presented with PVT within one year of implantation and the remaining patients (males: 9, females: 4) presented 1-3years since their valve replacement. On analysing the previous records, only 28 people were on regular follow up of once in a month and the remaining 20 patients were on less than 2 follow ups after their surgery.

Patients	Male	Female
48	35	13

Age range	25 – 48 years

Presentation of acute thrombotic occlusion	Male	Female
Less than 1 year	26	9
1 year to 3 years	9	4

Patient's profile	Male	Female
Rural	30	8
Semi urban	5	5

Follow ups	No of patients
Regular	28
Only 2 follow ups	20

Valves replaced	Males	Females
Mitral	20	10
Aortic	14	3
Double valve replacement(mitral and aortic)	1	0

Co morbid conditions	No of patients
Diabetes mellitus	1
Dyslipidemia	3
Tuberculosis	2

Co morbid conditions like dyslipidemia (3 patients), diabetes mellitus (1 patient), and tuberculosis (2 patients) were present. Acenocoumarol was the anticoagulant used for the patients. 38 patients (males: 28, females: 10) were on regular anticoagulant medications. 10 patients were on irregular medications. Various pattern of presentation were noted such as muffled clicks (48 patients), pulmonary edema (36 patients), class IV symptoms (43 patients), new onset off murmur (15 patients), chest pain (24 patients), hypotension (38 patients), atrial fibrillation (12 patients), fever (3 patients)

Intake of anti coagulants	Male	Female
INR 2.5 AND Above	8	2
INR less than 2.5	27	11

Pattern of presentation	Male	Female
Fever	2	1
Class 4 symptoms	32	11
Chest pain	14	10
Pulmonary oedema	28	8
Hypotension	30	8
New onset murmur	10	5
Atrial fibrillation	2	10
Muffled clicks	35	13

Complications	Male	Female
Fatal bleeding	2	1
Cerebral embolism	2	0

INR <2.5 predisposes to thrombosis. In our study 38 patients had INR <2.5, remaining 10 patients had valve thrombosis despite INR >2.5.

Out of 48 patients 34 (70.8%) patients underwent thrombolysis with Streptokinase. 14 (10 mitral and 4 aortic) patients underwent surgery

(29.2%). Thrombolysis was successful with return of full leaflet mobility in 22 patients (64.7%). Partial return of leaflet mobility in 7 patients (20.6%). 5 patients died of complications (14.7%). 60% (12/20) of patients had complete success following thrombolysis of mitral valve prosthesis, 77% (10/13) of patients had complete success following thrombolysis in aortic valve prosthesis. One patient with double valve replacement had thrombosis of mitral valve- underwent successful thrombolysis. Total mortality in our study is 7 (14.6%). 3 patients died of fatal bleeding, 2 patients died of Cerebral embolism and 2 patients out of 14 patients who underwent surgery died.

Figure shows gender profile

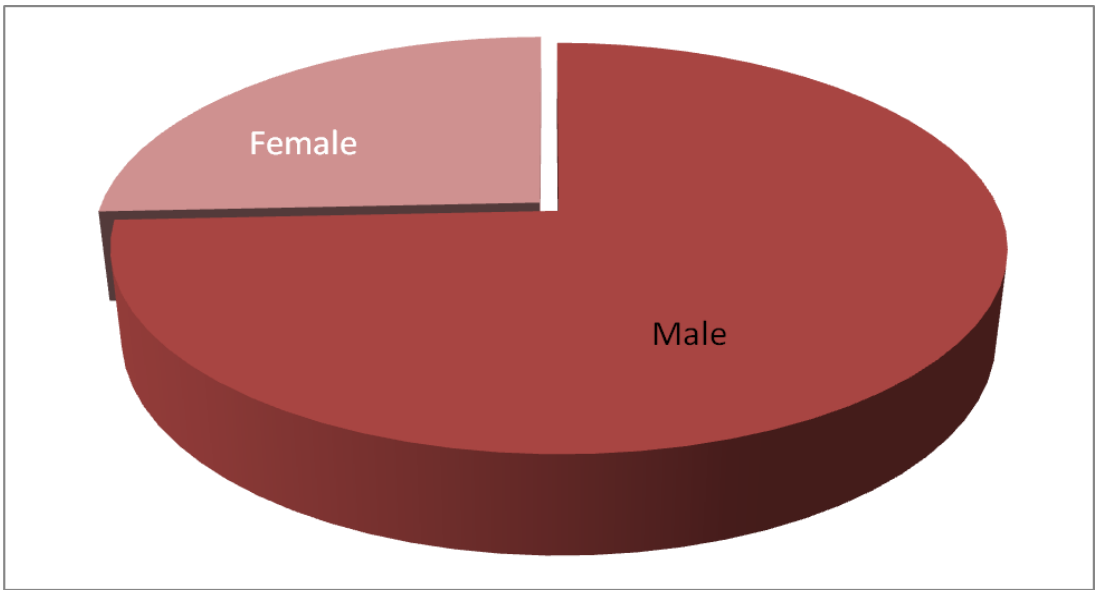


Figure shows timing of occurrence of valve thrombus following valve implantation

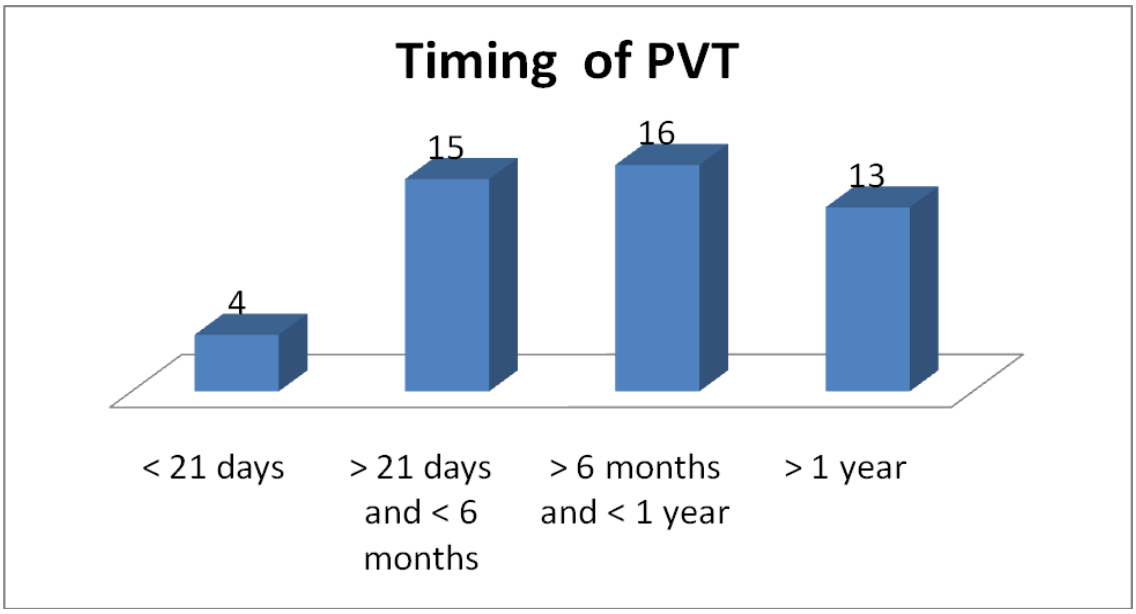


Figure showing follow up course of the patients after valve replacement

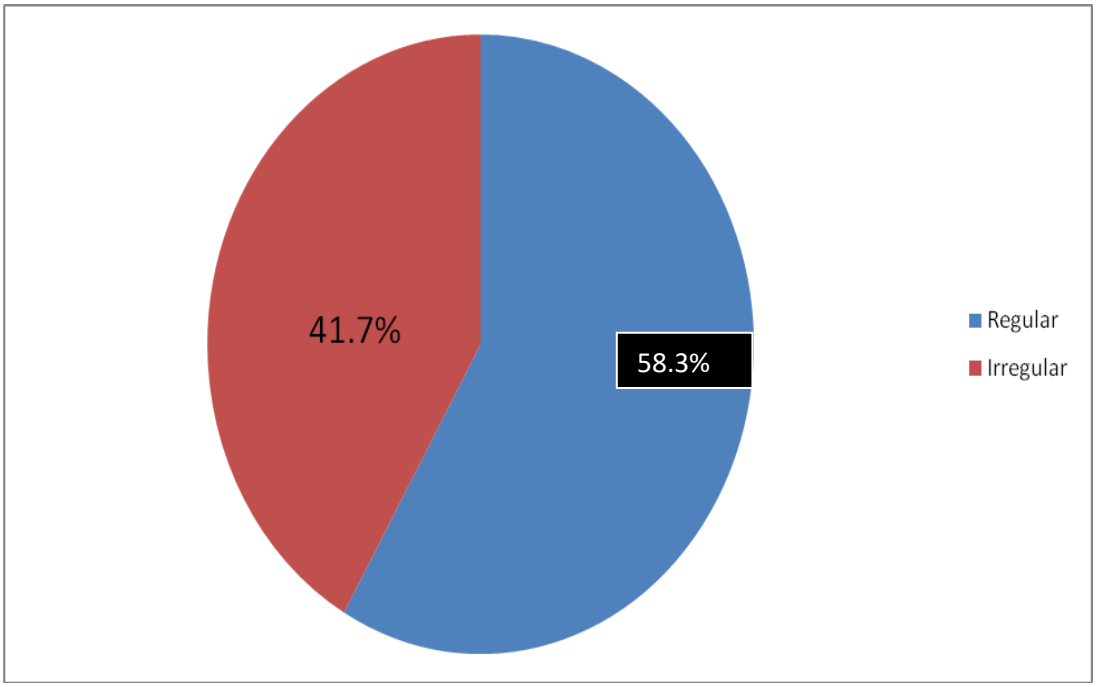


Figure shows level of anticoagulation in the patients

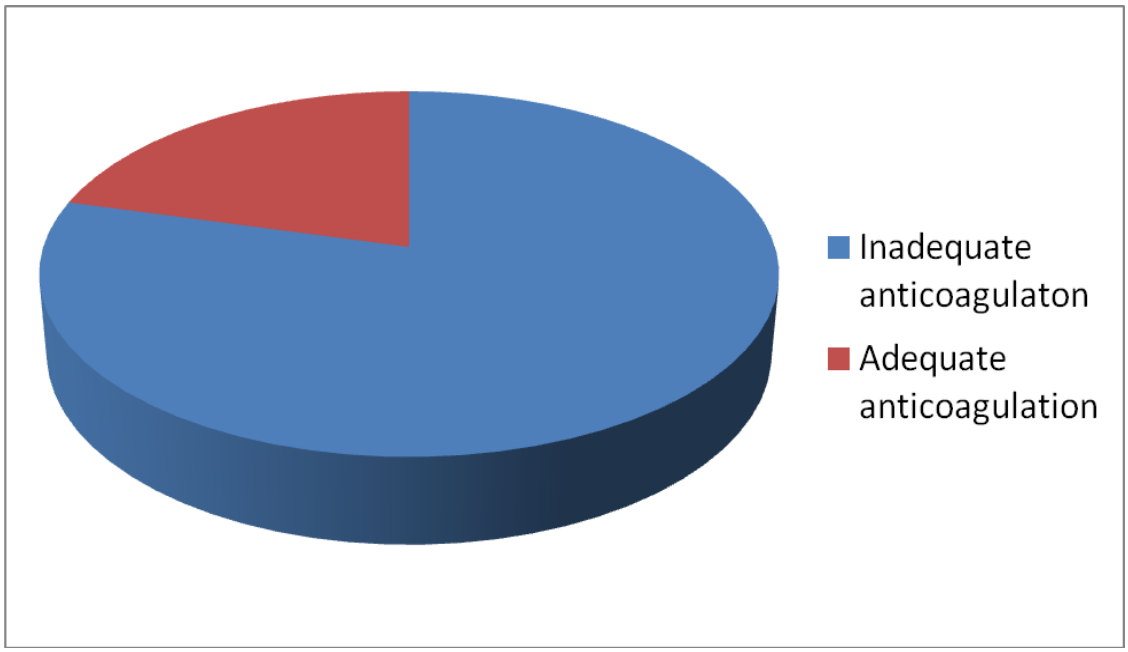


Figure shows incidence of thrombosis according to the valve location

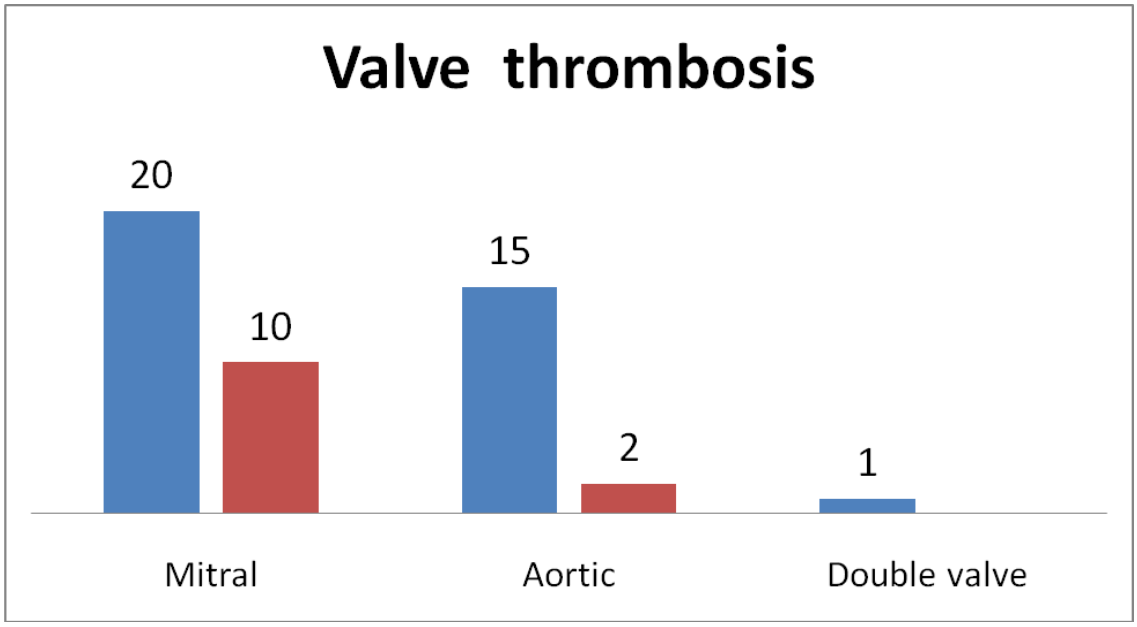


Figure shows the various causes of prosthetic valve thrombosis

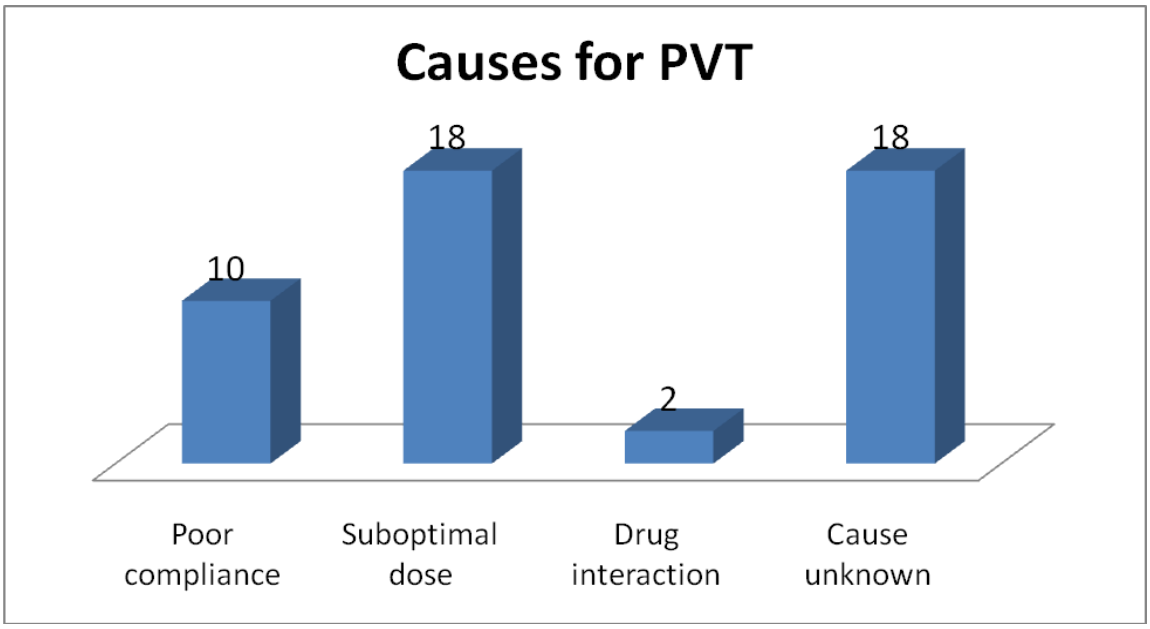


Figure shows clinical profile of the prosthetic valve thrombosis patients

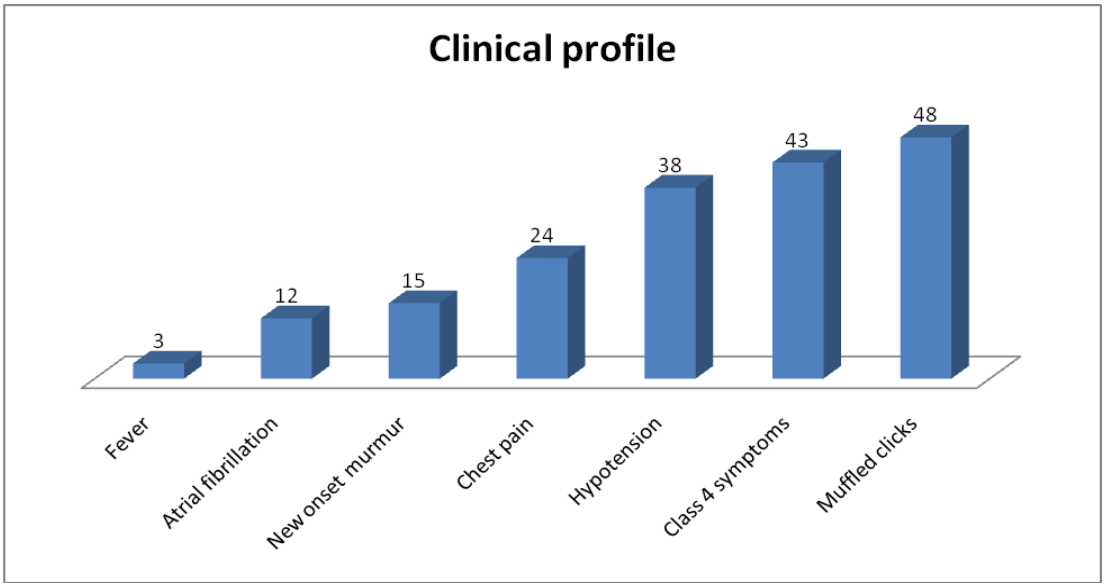


Figure shows percentage of patients with various levels of success of thrombolysis

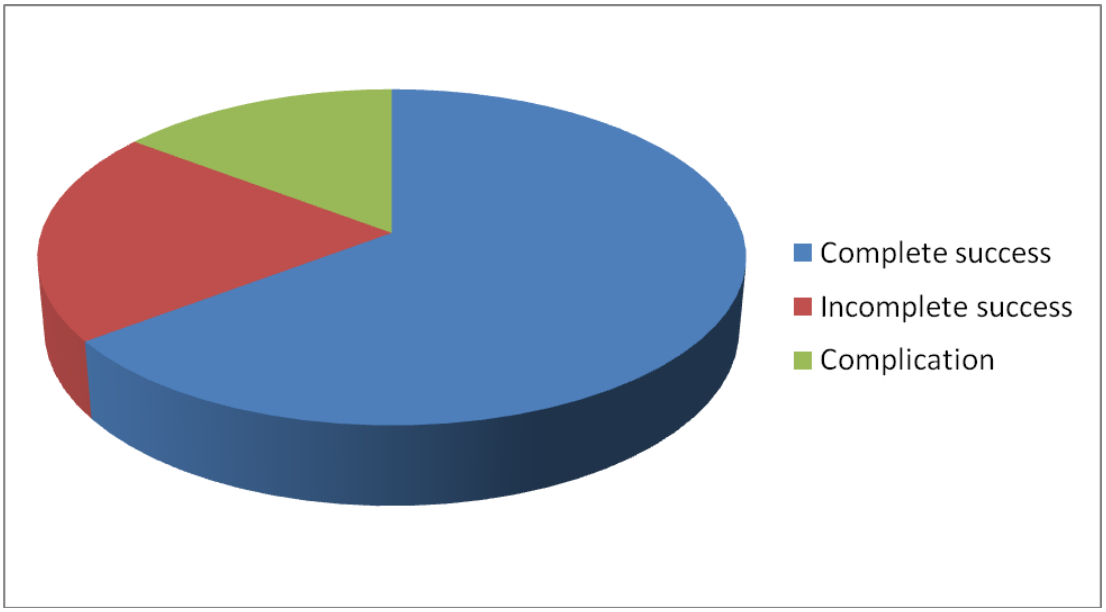


Figure shows successful thrombolysis according to location of thrombus:

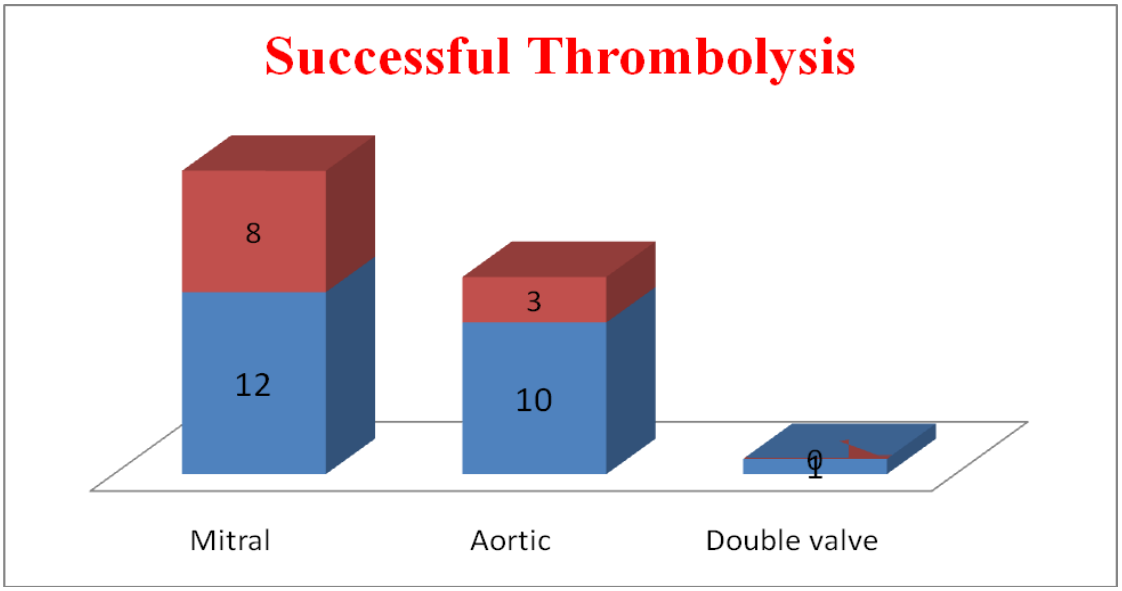


Figure shows echocardiographic parastrenal long axis view of thrombus in the mitral prosthetic valve

Figure shows echocardiographic parastrenal long axis view with colour flow doppler of thrombus in the mitral prosthetic valve

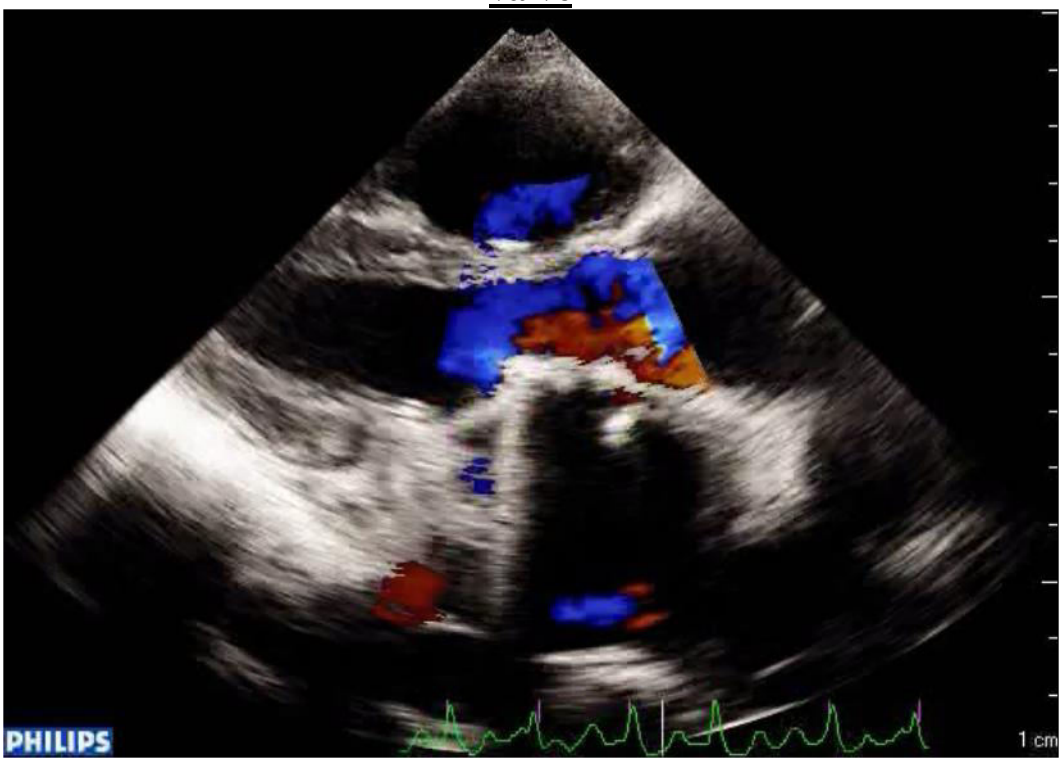


Figure shows echocardiographic parastrenal short axis view of thrombus in the mitral prosthetic valve

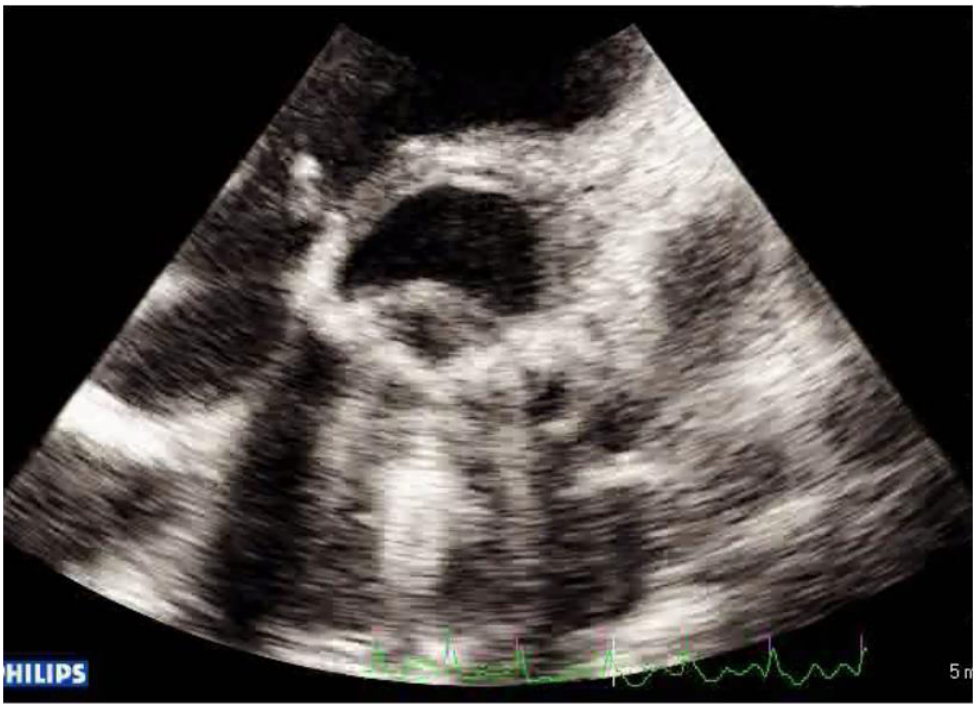


Figure shows increased flow gradient across mitral valve

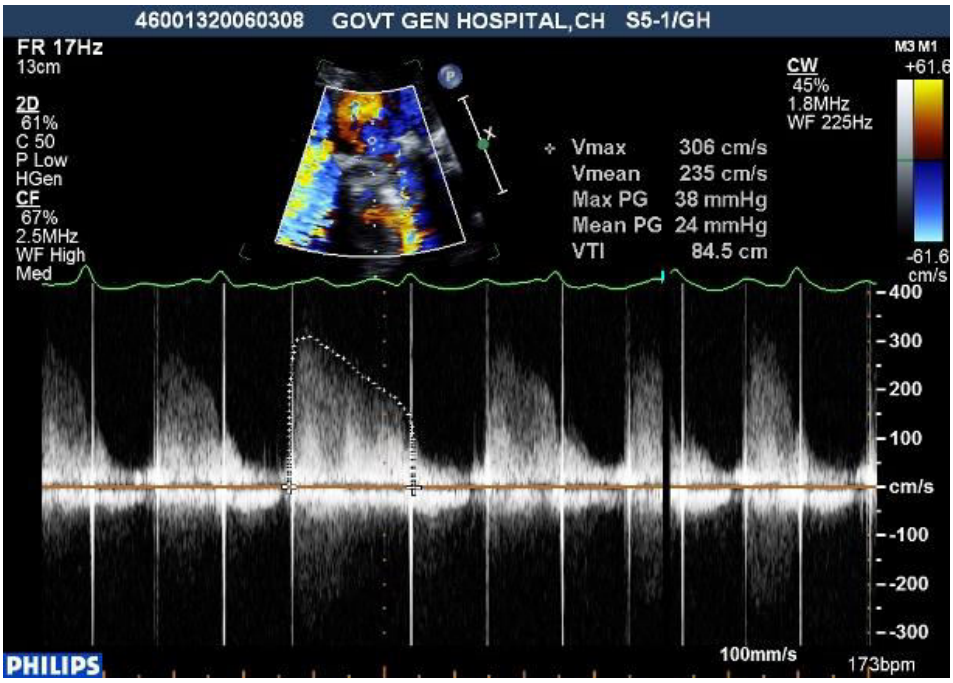
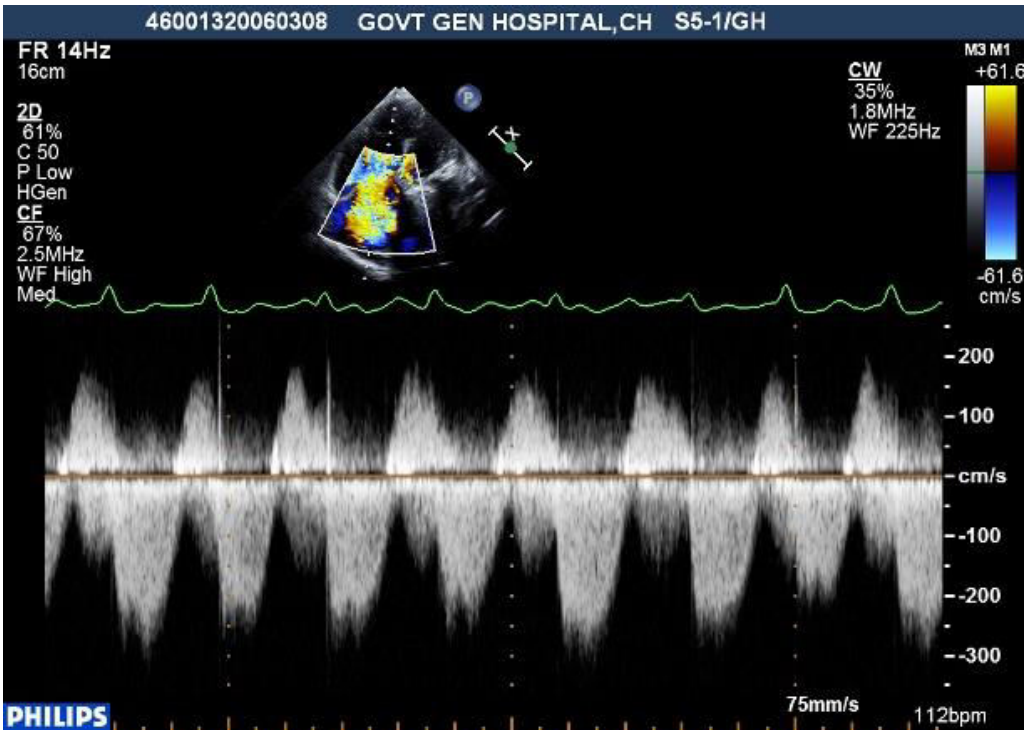
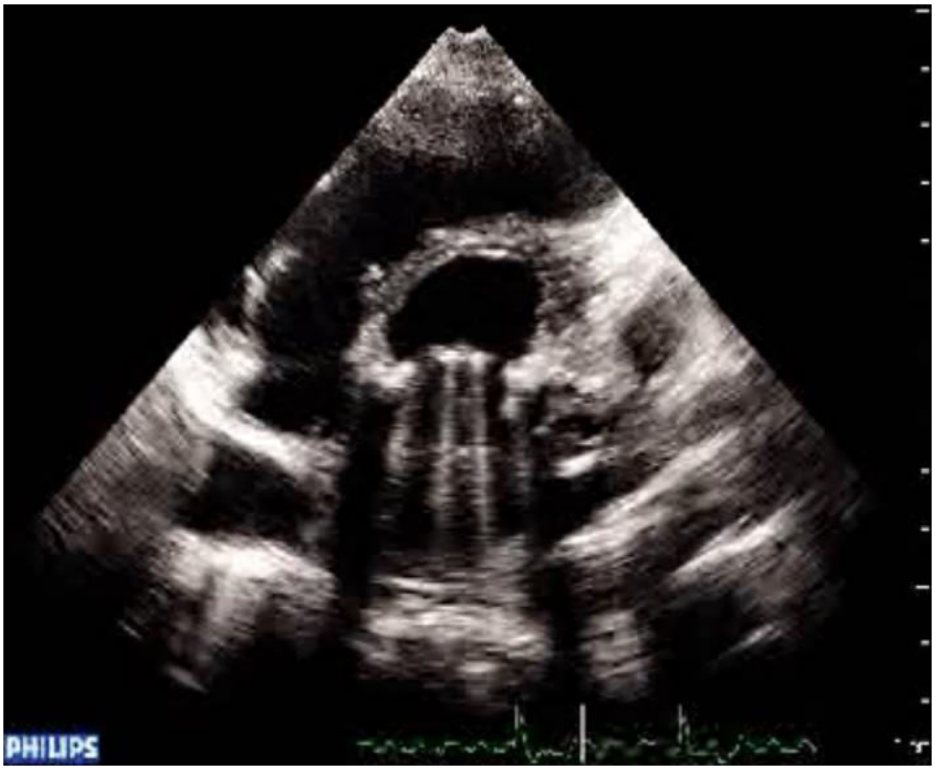


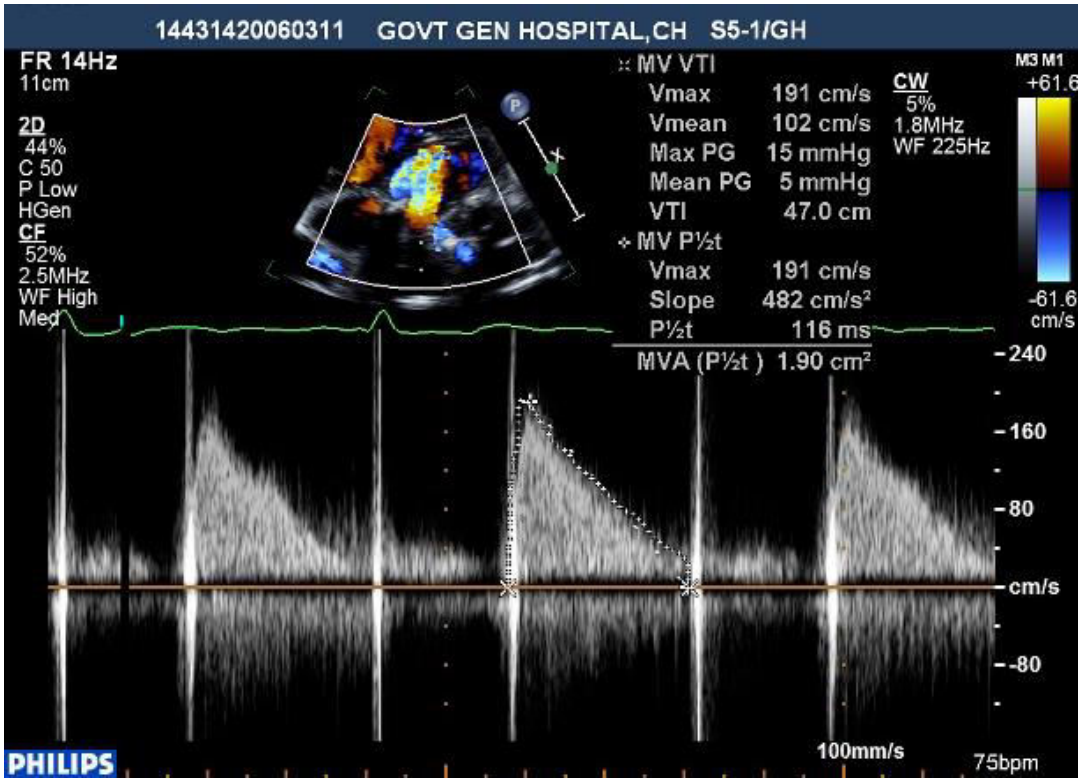
Figure shows severe tricuspid regurgitation and severe pulmonary hypertension



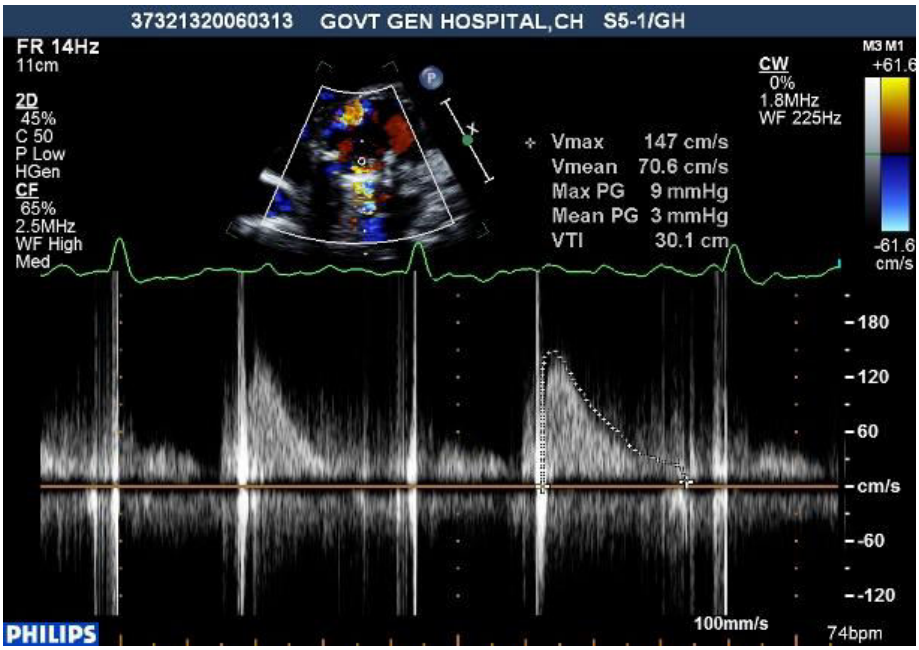
Figures showing echocardiography of opening of mitral prosthetic leaflet following successful thrombolysis



Figures showing decrement in gradients following thrombolysis at 24 hours



Figures showing decrement in gradients following thrombolysis at 48 hours



Fluoroscopic images showing opening of the prosthetic valve leaflets following thrombolysis

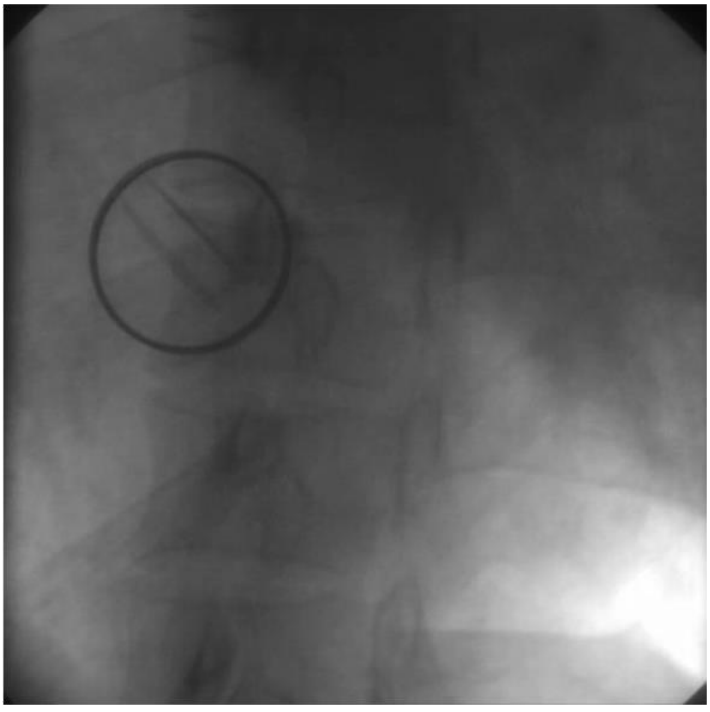
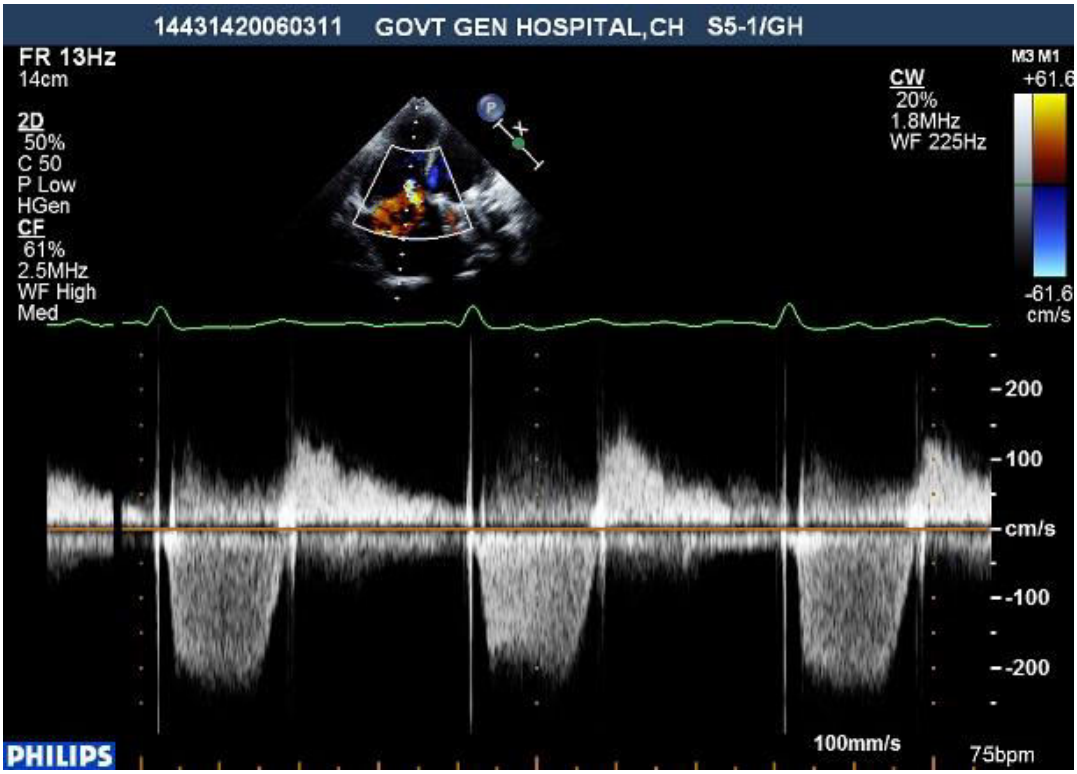


Figure shows reduction in tricuspid regurgitation and subsequent pulmonary hypertension



DISCUSSION

PVT is a life threatening situation. Prompt earlier diagnosis followed by rapid treatment will save the life. Management of severe rheumatic heart disease by prosthetic valve implantation does not mean the patient is cured. With the implantation of artificial valves, a disciplined protocol for follow up and maintenance of anticoagulation levels are the important task. With more than 3, 00,000 valve replacements done worldwide there arise a new group of patients called prosthetic valvular heart disease patients. These patients has to be managed with high levels of health education about the valves, about the anticoagulants, about the necessity of maintaining adequate INR levels and need for regular follow up, food habits etc.

In our study, all the 48 patients had bileaflet mechanical valve in various locations such as mitral, aortic. Majority of our patients were males and belong to rural areas in our study. Except for co morbid conditions such as diabetes, dyslipidemia and tuberculosis in a few patients, majority of our patients were free of associated diseases. About 73% of our patients presented with PVT within one year of valve replacement. Thus surgery related issues and post operative care, post operative monitoring of anticoagulation, follow up and importance of

maintaining INR levels are areas to be intervened. 2 patients had pulmonary tuberculosis and were taking anti tuberculosis drugs. Drug interaction of acenocoumarol with rifampicin could be a cause for low PT/INR in these patients.

Clinically all our patients had muffling or absence of prosthetic valve sounds. Most of the patients presented with pulmonary edema, class IV symptoms and hypotension. About 25% of patients had atrial fibrillation at presentation, which were new onset. Thus atrial fibrillation could be a predisposing factor. 3 of our patients had fever of high degree during presentation. Fever leading to dehydration could also be a contributor for PVT. In our study, about 63% of patients with PVT had prosthetic valve at mitral location and 35% had aortic prosthetic valve. Since prosthetic valve at mitral position is prone to thrombosis, our study also confirmed it

On analysing the records available with the patients we found that about 42% had infrequent follow up. Thus a greater emphasis should be placed on educating the patient for the need of follow up. 79% of our patients during presentation had INR of <2.5.Thus a major reason for PVT in our study is inadequate anticoagulation. Buttard and colleagues10 found inadequate systemic oral anticoagulation at the time of diagnosis in

45%: 27% for medical reasons (surgical intervention, neurologic events, or pregnancy) and 17% because of poor patient compliance. This is the vital area of care and lot of resources and man power is needed to overcome this major factor. Also 21% of our patients presented with PVT in spite of their INR being above 2.5 at the time of presentation. The probable reasons could be pannus rather than thrombus could be the reason for obstructive PVT or the reliability of INR as a measure of adequate anticoagulation is not superior. In our study 34 (70.8%) patients underwent thrombolysis with Streptokinase. Treatment options were decided according to the guidelines. And the thrombolytic therapy was given according to the protocols followed by heparin and warfarrin.

The recent review of Lengyel et al. of 200 published reports of left-sided prosthetic heart valve thrombolysis showed an 82% initial success rate, an overall thromboembolism rate of 12%, and a mortality rate of 10%. This consensus conference indicates that FT of left-sided PVT is acceptable for critically ill patients in whom surgical intervention carries high risk or in patients with contraindications to operation. Several studies have examined the role of thrombolysis in the management of PVT. Recently, Roudaut and coworkers conducted a retrospective study of 110 patients treated with fibrinolytic therapy and concluded that the treatment should be reserved for selected patients (those with tricuspid

thrombosis, critically ill patients, and patients with contraindications to surgical intervention).

Thrombolysis was successful with return of full leaflet mobility in 22 patients (64.7%). Partial return of leaflet mobility in 7 patients (20.6%). 5 patients died of complications (14.7%) in our study. When analyzed the success of thrombolytic therapy according to valve location it has been found that 60% (12/20) had complete success following thrombolysis of mitral valve prosthesis and 77% (10/13) complete success following thrombolysis in aortic valve prosthesis. One patient with double valve replacement had thrombosis of mitral valve- underwent successful thrombolysis. So, overall thrombolysis is better treatment alternative to surgery in many patients for whom surgery could not be performed. 5(about 15%) patients who were in the thrombolysis arm died due to bleeding complication (3 patients) and cerebral embolism (2 patients).

14 (10 mitral and 4 aortic) patients underwent surgery (29.2%). Surgery was done in the form of simple thrombectomy in 8 patients (57%) and valve replacement in remaining 6 patients (43%). 2(14%) patients who underwent valve replacement died.

Patients with PVT have high mortality. The commonest predisposing factors for PVTs are inadequate anticoagulation and poor patient compliance. Thus underscoring the need for both patient- and physician-oriented education. Thrombolysis is a reasonable and valid alternative therapy. Surgical intervention may be needed in many patients with PVT. In short regular follow up, periodic monitoring of INR and adjusting it to the ideal level and stable diet pattern play important role in preventing complications of prosthetic valves. And in today's world where there is excellent communication facilities, patients can be followed up through phone where the dose of the patient's anticoagulants can be modified according to the INR levels which they can see in their native place and communicate to the doctors through phone.

CONCLUSION

- The incidence of PVT is higher and is about 1.2 per 1000 patient years.

- The major risk factors for PVT observed in our study are inadequate anticoagulation, lack of follow up and patient prosthesis mismatch.

- Regarding treatment thrombolysis is a reasonable alternative for surgery with nearly 80% success rate.

As the rheumatic heart disease is very much prevalent in India, prosthetic heart valves implantation rate is increasing every year due to high incidence of RHD in India. Inadequate anticoagulation, lack of follow up, non compliance, lack of health education continues to be the major factors for PVT.

Technical and lesion related factors are also important as many cases present early after surgery. So, special care should be taken to avoid patient prosthetic mismatch.

Clinical recognition of PVT still plays a vital role, as subtle signs like increase in dyspnea and muffling of clicks may picked up at bedside and leads to suspicion of PVT.

Diagnostic tools such as echocardiography (TTE, TEE) play a vital role in diagnosis of PVT through detection of increased gradients and appearance of new regurgitation and visualization of mobility of leaflets.

Thrombolytic therapy can be considered as an effective initial intervention (In spite of being class IIb indication as per AHA).

Surgery should be recommended for valve dehiscence, large thrombus and for those patients having contraindications to thrombolysis. Emergency cardiac surgery cannot be advocated in most due to logistic reasons.

Patient education & better communication are the best tools for prevention of PVT. Physicians need to be aware of various drug interactions with anticoagulants such as warfarrin and acenocoumarol.

Patients need to be educated about the importance of periodic monitoring of INR and adjusting it to the ideal level. They also need to be educated about the anticoagulants and to be taught about subtle signs of bleeding and early signs of PVT.

Finally, in the era of advancement in communication systems patient doctor relation can be improved and will play a crucial role in anticoagulation maintenance and thus preventing prosthetic valve thrombosis.

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ABBREVIATIONS

PVT	-	Prosthetic Valve Thrombosis
ECG	-	Electrocardiogram
TTE	-	Trans Thoracic Echocardiogram
TEE	-	Trans Esophageal Echocardiogram
NYHA	-	New York Heart Association
EOA	-	Effective Orifice Area
ACC/AHA	-	American College Of Cardiology/ American Heart Association
rTPA	-	Recombinant tissue plasminogen activator
Mg	-	Milligram
MM	-	Millimetre
IU	-	International unit
OC	-	Opening Click
CC	-	Closing Click
MHz	-	Mega Hertz
VTI PrMV	-	Velocity Time Integral Prosthetic Mitral Valve
VTI LVO	-	Velocity Time Integral Left Ventricular Outflow Tract
PHT	-	Pressure Half Time
AT	-	Acceleration Time
PT/INR	-	Prothrombin Time/ International Normalised Ratio

PROFORMA

Name

Age

sex

Address

Occupation

Education

Type of valve

Duration since valve implantation

Clinical parameters

Pulse rate

Respiratory rate

Spo2

Systolic blood pressure

Diastolic blood pressure

Cardiovascular examination

Heart / prosthetic valve sounds

Other system examination

Co morbid conditions

Diabetes

Systemic hypertension

Renal failure

Tuberculosis

Malignancies

HIV

Heart failure

Pericardial effusion

INVESTIGATIONS

Biochemical

Haemoglobin

Blood sugar

Urea

Serum creatinine

Lipid profile

Liver function test

Prothrombin time/INR

Peripheral smear

Bleeding time

Clotting time

Electrocardiography

Echocardiography

Trans thoracic echo

Trans esophageal echo

Fluoroscopy